REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that Claims 1-47 are pending in the application. Claims 3-5 and 8-47 stand withdrawn from consideration subject to restriction requirement. Claims 1, 2, 6 and 7 are under consideration and stand rejected.

By the present amendment, Claim 6 is rewritten to more clearly describe the claimed subject matter. Support for the amendments to Claim 6 may be found throughout the specification and at least in Claim 6 as previously presented.

Claims 48-61 have been added. Support for the added claims can be found throughout the Specification and the Claims as originally filed, for example, in the Specification at least at pages 106-107 and 116.

Formal Drawings are submitted concurrently herewith. The Formal Drawings correct the defects in matters of form noted on Form PTO-948 that was attached to Paper No. 17 with respect to the Drawings as originally filed. The number of sheets has changed in order to accommodate changes in font size and the arrangement of views in some figures.

A Substitute Sequence Listing in paper and computer readable forms is submitted herewith. The substitute Sequence Listing incorporates sequences disclosed in the Specification as originally filed, which were omitted from the Sequence Listing as originally filed.

The Specification has been amended to reflect changes to the number of sheets of drawings and to incorporate appropriate sequence identifiers.

No prohibited new matter is believed to have been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application directed to any subject matter canceled by way of this Amendment.

Election

Applicants election **with traverse** of Group I, Claims 1, 2, 6 and 7, and the species SEQ ID NO:1 in Claim 6 has been acknowledged, and the restriction requirement has been made final. Applicants reserve the right to petition for review of the restriction requirement pursuant to 37 C.F.R. § 1.144.

Drawings

Corrected Drawings have been required for the reasons set forth on the form PTO-948 attached to Paper No.17. Formal drawings, correcting the noted deficiencies, are submitted concurrently herewith.

Sequence Listing

A substitute Sequence Listing has been required because the Specification, as originally filed, contains sequence disclosures that are not designated with appropriate sequence identifiers and certain sequences were inadvertently omitted from the original Sequence Listing. By the present amendment, the Specification is amended and a substitute Sequence Listing, in paper and computer readable forms, is submitted in accordance with 37 C.F.R. §§ 1.821-825.

Priority

Applicants' claim for domestic priority under 35 U.S.C. § 119(e) and 120 is acknowledged. However, the Office asserts that the provisional applications upon which priority is claimed do not provide adequate support under 35 U.S.C. § 112 for the elected claims. In particular, the Office alleges that the provisional applications do not disclose the sequences of Zmax1, HBM, or the polymorphisms of Zmax1/HBM encompassed by the claims.

Applicants point out that Provisional Application No: 60/071,449 discloses, *inter alia*, the BAC clone DNA molecule B200E21-H and its deposition in the American Type Culture Collection (ATCC) under accession number 98628. The Provisional Application No: 60/105,511 further discloses, *inter alia*, the BAC clone DNA molecule B527D12-H and its

deposition in ATCC under accession number 98907. These BAC clones comprise the Zmax1 gene. The Provisional Patent Applications describe the localization of the gene related to the HBM phenotype to the sequences of these BAC clones.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 6 and 7 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, because step (C) indicates that a single molecule is identified in steps (A) and (B). Steps (A) and (B) describe identifying a molecule that binds to SEQ ID NO:1 and SEQ ID NO:2, respectively. As amended, Claim 6 is rewritten to more clearly recite the claimed subject matter. In Claim 6, as amended, it can be clearly recognized that the same first kind of molecule, and optionally a second kind of molecule (whose binding to the recited sequences may be inhibited by the first kind of molecule), is referred to in each of steps (A), (B) and (C).

Applicants believe that one of skill in the art would understand the meets and bounds of the presently claimed invention. One of skill in the art would recognize that the singular of the term "a molecule" as used in the present claims refers to a single substance, molecule or element, and includes a plurality of atoms or molecules of the same substance or molecular formula. One of skill in the art would immediately recognize that binding measurements are most commonly performed upon ensembles of elements or molecules of putative ligands and substrates. Further, one of skill in the art would recognize that only when the molecule identified in step (A) was the same as the molecule identified in step (B) could the comparison of step (C) be carried out.

Applicants have amended Claim 6 to more clearly recite the claimed invention. Claim 6, as amended, describes a method in which a first molecule is identified which binds, or inhibits the binding of a second molecule, to either a Zmax1 nucleic acid or a HBM nucleic acid in step (A); that the binding of this first molecule or its inhibition of binding of the second molecule with the other of either the Zmax1 or HBM sequences is measured in step (B); and that the relative binding of the first molecule or its inhibition of binding of the second molecule to the HBM and Zmax1 sequences is compared in step (C).

The scope of Claim 6 is unchanged by the present amendment. In Claim 6, as originally filed, step (A) was the identification of a molecule that binds to, or inhibits another molecule from binding a Zmax1 sequence. Step (B) was the identification of a molecule that binds to, or inhibits another molecule from binding a HBM sequence. Steps (A) and (B) of Claim 6, as originally filed, could occur in any order. Step (C) comprises comparing the binding or inhibition of steps (A) and (B). Claim 6, as amended, describes the same process.

Claim 6 as amended clearly recites the claimed subject matter such that one of skill in the art can recognize the meets and bounds of the invention. Accordingly, withdrawal of the rejection of Claim 6, and dependent Claim 7, under 35 U.S.C. § 112, second paragraph is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1 and 2 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the Specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed. Specifically, the Official Action asserts that the recitations of HBM and Zmax1 in Claim 1 encompass variants and polymorphisms that were not described in the Specification. The rejection is respectfully traversed.

The HBM and Zmax1 genes and proteins are clearly defined in the Specification and are described in a manner that is more than sufficient to indicate to one of skill in the art that the inventors were in possession of the invention, as claimed, at the time the application was filed. For example, Zmax1 is clearly defined at least at page 19, lines 3-8. The *Zmax1* gene comprises the nucleic acid sequence SEQ ID NO: 1 and can also refer to allelic variants of the gene that do not contribute to the HBM phenotype. Thus, Zmax1 refers to the genus of variants of the Zmax1 sequence exemplified by SEQ ID NO:1 and polymorphisms of SEQ ID NO:1 that result in a normal bone mass phenotype. A representative number of variants of Zmax1, identified in various subjects, are shown in Table 4 of the specification. In light of at least the above and the substantial amount of sequence information provided in the Specification, the rejection for alleged lack of written description of Zmax1 and HBM is inappropriate.

HBM is defined, for example, at page 18, line 15 to page 19, line 2. A human HBM protein is identical to a human Zmax1 protein with the exception of the alteration of glycine 171 to valine. The difference in the genomic sequence of HBM gene as a variant of the Zmax1 gene is described, for example at page 73, lines 13-21 and in Table 4. An HBM protein is also defined for any organism that has a true Zmax1 homolog. For example, a mouse HBM protein refers to the mouse Zmax1 homolog having a glycine 170 to valine substitution. The protein encoded by the HBM gene has the property of causing elevated bone mass and also altering physiologic lipid levels while the protein encoded by Zmax1 does not.

The Official Action alleges that the disclosed variants are not a representative number. The Official Action further alleges the Specification fails to describe common elements or attributes of the sequences or even the presence of certain domains. However, many common structural elements of the Zmax1 variants are described such that one of skill in the art would be able to recognize a variant of Zmax1. For example, Figure 4 shows a schematic of the Zmax1 protein including the identity and sequential coordinates of domains that characterize a Zmax1 protein. The identification of characteristic domains also conveys secondary and tertiary structural information to one of skill in the art. The identification and analysis of a number of polymorphisms of the HBM and Zmax1 gene are described in detail, for example, at pages 69-74 of the specification.

The Official Action cites *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) in support of the rejection. However, the present application is more analogous to the situation in *Amgen Inc. v. Hoechst Marion Roussel*, which was recently decided by the Federal Circuit. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, No. 01-1191,-1218 (Fed. Cir. Jan. 6, 2003) *available at* http://pub.bna.com/ptcj/011191.htm. In *Lilly*, the Federal Circuit upheld a determination of invalidity in the case where an application disclosed only a rat cDNA of insulin, the peptide sequence of human insulin A and B chains, and a method for obtaining the human cDNA. The application in *Lilly* provided no information regarding the claimed human cDNA. The Court held that to satisfy the written description requirement for a claimed DNA, requires a "precise definition, such as by

structure, formula, chemical name, or physical property." *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d at 1404.

The present case is substantially distinct from the facts of *Lilly*. In the present specification, complete exemplary sequences of Zmax1 are described in its genomic, cDNA, and protein sequences. In addition, a representative number of normal or wild-type variants of the exemplary sequence are described. These variants are found individually, or in combination, to correspond to a normal, un-affected phenotype. Characteristic domain organization and recognizable motifs of Zmax1 proteins are described. Moreover, the location of the Zmax1 gene on human chromosome 11q13 is described.

With respect to the HBM variant of Zmax1, the specific structural difference between HBM and Zmax1 is described in terms of its genomic, cDNA, and protein sequence. Distinguishing physiological effects of the Zmax1 and HBM genes are described. Exemplary data and analysis are provided that will allow one of skill in the art to distinguish the HBM phenotype from the normal Zmax1 phenotype, for example, in terms of bone and lipid parameters. In *Lilly*, a novel DNA sequence was claimed, but only a functionally descriptive name and a means of obtaining the sequence were disclosed in the specification for the claimed gene. *Id.* at 1405.

Here, as in *Amgen Inc. v. Hoechst Marion Roussel*, the claims under consideration refer to biological material, but do not claim the biological material itself. The claims under consideration are directed to methods for using biological material. Sequences denoted by the names Zmax1 and HBM that can be used in the claimed methods are defined in the specification by multiple examples of a specific primary structure and exemplary variants as well as by description of the domain organization of the Zmax1 protein shown in Figure 4. Proteins encoded by the Zmax1 and HBM genes are further described by secondary and tertiary structural parameters inherent in the description of the domain organization and by functional properties.

Therefore, it cannot be true that the present disclosure represents only a mere wish or plan to obtain the claimed sequences. In the present specification, one of skill in the art is provided more than enough description of Zmax1 and HBM to understand the biological material that can be used in the claimed methods. One of skill in the art would not be likely

to mistake the recited biological material. The Federal Circuit has recently held that where a claim refers to biological material that would be understood by one of skill in the art, the claim is not invalid under 35 U.S.C. § 112, first paragraph. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, No. 01-1191,-1218 (Fed. Cir. Jan. 6, 2003) *available at* http://pub.bna.com/ptcj/011191.htm. The Federal Circuit held that the standard set forth in *Lilly* simply does not apply. *Id.* In view of the extensive description provided by the present Specification, an overly rigid application of *Lilly* to require an exhaustive recitation of every functionally equivalent variant of Zmax1 or HBM is inappropriate.

Accordingly, withdrawal of the rejection of Claims 1 and 2 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1 and 2 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Dong et al. (*Biochem. Biophys. Res. Com.*, 251:785-90, 1998) in view of Fields et al. (U.S. Patent No. 5,283,173). The rejection is respectfully traversed as failing to set forth a *prima facie* case of obviousness.

Dong et al. describes a protein, designated LR3, with homology to Zmax1. Dong et al. identifies LR3 as a member of the LDL receptor family of proteins. Fields et al. teaches a method of detecting protein-protein interactions. It is asserted in the Official Action that the LDL receptor family was known to be involved in lipid regulation. It is also asserted that it would have been obvious to combine the teaching of Fields et al. with the teaching of Dong et al. to create a method of identifying molecules involved in lipid regulation. It is further asserted that the motivation to do so would derive from the teaching by Dong et al. that LR3 is a member of the LDL receptor family of proteins.

However, the assertion of a motivation to combine the references is in error. There is no suggestion in Dong et al. to combine the teachings thereof with the method of Fields et al. The rejection does not fully characterize the teachings of Dong et al., which actually lead away from the claimed invention.

The teachings of Dong et al. do not suggest that LR3 is involved in lipid regulation in any way. In fact, the teachings of Dong et al. suggest some other role for LR3. Dong et al.

note that LR3, unlike all the other members of the LDL receptor family does not have the NPXY internalization motif of the LDL receptor. This motif is critical to the lipid uptake function of the LDL receptor. *See*, Dong et al. at page 787, 2nd col. 788, 2nd col. , and Fig. 5. Dong et al. note other properties of LR3 that are not seen in members of the LDL receptor family. For example, the arrangement of domains in LR3 is substantially different than the arrangement of domains in the members of the LDL receptor family that are directly involved in lipid regulation. *See*, Dong et al. at page 789, Fig 5. Furthermore, the members of the LDL receptor family have a wide array of apparent functions. While, the LDL receptor primarily binds lipoproteins, many structurally and functionally diverse ligands have been identified for different members of the LDL receptor family. *See*, Dong et al. at page 784. Therefore, the known functions of the LDL receptor family are not exclusively related to lipid regulation. Dong et al. teach that no known LDL receptor family ligands have been tested on LR3. *See*, Dong et al. at page 789. So there is no actual data regarding the ligands of LR3. Dong et al. conclude their discussion of LR3 with the statement that, "[T]he unique position of the ligand binding repeats in LR3 and the lack of an internalization signal and the Ca2+ binding activity . . . all lead us to speculate that LR3, instead of being a new receptor mediating endocytosis of lipoproteins, may interact with ligand(s) of different biochemical activity. See, Dong et al. at page 790.

From the foregoing, it is apparent that Dong et al. convey a substantial doubt that the function of LR3 relates in any way to the lipid regulating function of the LDL receptor. Accordingly, the teachings of Dong et al. provide no motivation to create a method of identifying a molecule involved in lipid regulation comprising identifying a molecule that binds to, or that inhibits binding of a molecule to Zmax1 or HBM. In fact, the teachings of Dong et al. lead one of skill in the art away from the claimed invention. The reference itself contradicts the motivation suggested in the rejection.

There is no suggestion in Fields et al. of applying the disclosed method to LR3 or any related protein, there is no suggestion that the method may be applied to the identification of a molecule involved in lipid regulation. The teaching of Dong et al., discussed above, fails to cure the defects inherent in Fields et al. Thus, neither reference considered alone or in combination suggests the claimed invention.

Even if all the elements of the claimed invention could be identified in Dong et al. and Fields et al., the combination cannot be found obvious in the absence of some motivation to make the combination. Most if not all inventions arise from a combination of old elements. *See, In re Rouffet,* 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1457 (Fed. Cir. 1998). Thus, every element of a claimed invention may often be found in the prior art. See, *Id.* However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. See, *Id.* Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. *In re Kotzab*, 217 F.3d 1365, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000) (citing *In re Dance*, 160 F.3d 1339, 1343, 48 U.S.P.Q.2d 1635, 1637 (Fed. Cir. 1998); *In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984)).

Dong et al. contradicts the motivation to make the proposed combination that is asserted in the rejection. Consequently, the Official Action does not set forth a *prima facie* case of obviousness. *See,* M.P.E.P. § 2143. Accordingly, withdrawal of the rejection of Claims 1 and 2 under 35 U.S.C. § 103 is respectfully requested.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any issues relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such issues so that prosecution of this application may be expedited.

Respectfully submitted,

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By: _____

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Date: February 3, 2003

Attachment to the Response Dated February 3, 2003
Marked-Up Amendments

IN THE SPECIFICATION

Please replace the paragraph at page 11, lines 16-21, as follows:

[**Fig. 1** shows] **Figs. 1A and 1B** show the pedigree of the individuals used in the genetic linkage studies. Under each individual is an ID number, the z-score for spinal BMD, and the allele calls for the critical markers on chromosome 11. Solid symbols represent "affected" individuals. Symbols containing "N" are "unaffected" individuals. DNA from 37 individuals was genotyped. Question marks denote unknown genotypes or individuals who were not genotyped.

Please replace the paragraph at page 11, line 22 to page 12, line 10, as follows:

[**Fig. 2** depicts] **Figs. 2A and 2B** depict the BAC/STS content physical map of the HBM region in 11q13.3. STS markers derived from genes, ESTs, microsatellites, random sequences, and BAC endsequences are denoted above the long horizontal line. For markers that are present in GDB the same nomenclature has been used. Locus names (D11S####) are listed in parentheses after the primary name if available. STSs derived from BAC endsequences are listed with the BAC name first followed by L or R for the left and right end of the clone, respectively. The two large arrows indicate the genetic markers that define the HBM critical region. The horizontal lines below the STSs indicate BAC clones identified by PCR-based screening of a nine-fold coverage BAC library. Open circles indicate that the marker did not amplify the corresponding BAC library address during library screening. Clone names use the following convention: B for BAC, the plate, row and column address, followed by -H indicating the HBM project (i.e., B36F16-H).

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Marked-Up Amendments

Please replace the paragraph at page 13, lines 8-12, as follows:

Figs. 6A-[6E]6J [are] show the nucleotide and amino acid sequences (SEQ ID NOS: 1 and 3) of the wild-type gene, Zmax1. The location for the base pair substitution at nucleotide 582, a guanine to thymine, is underlined. This allelic variant is the *HBM* gene. The *HBM* gene encodes for a protein with an amino acid substitution of glycine to valine at position 171. The 5' untranslated region (UTR) boundaries bases 1 to 70, and the 3' UTR boundaries bases 4916-5120.

Please replace the paragraph at page 13, lines 17-18, as follows:

[Fig. 10 is] Figs. 10A and 10B show the cellular localization of mouse Zmax1 by *in situ* hybridization at 100X magnification using sense and antisense probes.

Please replace the paragraph at page 13, lines 19-20, as follows:

[Fig. 11 is] Figs. 11A and 11B show the cellular localization of mouse Zmax1 by *in situ* hybridization at 400X magnification using sense and antisense probes.

Please replace the paragraph at page 13, lines 21-22, as follows:

[Fig. 12 is] Figs. 12A and 12B show the cellular localization of mouse Zmax1 by *in situ* hybridization of osteoblasts in the endosteum at 400X magnification using sense and antisense probes.

Attachment to the Response Dated February 3, 2003
Marked-Up Amendments

Please replace the paragraph at page 75, lines 4-14, as follows:

The allele specific oligonucleotides (ASO) were designed with the polymorphism approximately in the middle. Oligonucleotides were phosphate free at the 5'end and were purchased from Gibco BRL. Sequences of the oligonucleotides are:

2326 Zmax1.ASO.g: AGACTGGGGTGAGACGC (SEQ ID NO: 63)

2327 Zmax1.ASO.t: CAGACTGGGTTGAGACGCC (SEQ ID NO: 64)

The polymorphic nucleotides are underlined. To label the oligos, 1.5 µl of 1 µg/µl ASO oligo (2326.Zmax1.ASO.g or 2327.Zmax1.ASO.t), 11 µl ddH_2O, 2 µl 10X kinase forward buffer, 5 µl γ-^{32}P-ATP (6000 Ci/mMole), and 1 µl T4 polynucleotide kinase (10 U/µl) were mixed, and the reaction incubated at 37°C for 30-60 minutes. Reactions were then placed at 95°C for 2 minutes and 30 ml H_2O was added. The probes were purified using a G25 microspin column (Pharmacia).

Please replace the paragraph at page 77, line 8 to page 78, line 8, as follows:

The sequence of the human and mouse PCR primers and products were as follows:

Human Zmax1 sense primer (HBM1253) (SEQ ID NO: 65)

CCCGTGTGCTCCGCCGCCCAGTTC

Human Zmax1 antisense primer (HBM1465) (SEQ ID NO: 66)

GGCTCACGGAGCTCATCATGGACTT

Human Zmax1 PCR product (SEQ ID NO: 67)

CCCGTGTGCTCCGCCGCCCAGTTCCCCTGCGCGCGGGGTCAGTGTGTGGACCTGCGCCTGCGC
TGCGACGGCGAGGCAGACTGTCAGGACCGCTCAGACGAGGTGGACTGTGACGCCATCTGCCTG
CCCAACCAGTTCCGGTGTGCGAGCGGCCAGTGTGTCCTCATCAAACAGCAGTGCGACTCCTTC
CCCGACTGTATCGACGGCTCCGACGAGCTCATGTGTGAAATCACCAAGCCGCCCTCAGACGAC
AGCCCGGCCCACAGCAGTGCCATCGGGCCCGTCATTGGCATCATCCTCTCTCTCTTCGTCATG
GGTGGTGTCTATTTTGTGTGCCAGCGCGTGGTGTGCCAGCGCTATGCGGGGGCCAACGGGCCC
TTCCCGCACGAGTATGTCAGCGGGACCCCGCACGTGCCCCTCAATTTCATAGCCCCGGGCGGT
TCCCAGCATGGCCCCTTCACAGGCATCGCATGCGGAAAGTCCATGATGAGCTCCGTGAGCC

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Mouse Zmax1 Sense primer (HBM1655) (SEQ ID NO: 68)

AGCGAGGCCACCATCCACAGG

Mouse Zmax1 antisense primer (HBM1656) (SEQ ID NO: 69)

TCGCTGGTCGGCATAATCAAT

Mouse Zmax1 PCR product (SEQ ID NO: 70)

AGCAGAGCCACCATCCACAGGATCTCCCTGGAGACTAACAACAACGATGTGGCTATCCCACTC
ACGGGTGTCAAAGAGGCCTCTGCACTGGACTTTGATGTGTCCAACAATCACATCTACTGGACT
GATGTTAGCCTCAAGACGATCAGCCGAGCCTTCATGAATGGGAGCTCAGTGGAGCACGTGATT
GAGTTTGGCCTCGACTACCCTGAAGGAATGGCTGTGGACTGGATGGGCAAGAACCTCTATTGG
GCGGACACAGGGACCAACAGGATTGAGGTGGCCCGGCTGGATGGGCAGTTCCGGCAGGTGCTT
GTGTGGAGAGACCTTGACAACCCCAGGTCTCTGGCTCTGGATCCTACTAAAGGCTACATCTAC
TGGACTGAGTGGGGTGGCAAGCCAAGGATTGTGCGGGCCTTCATGGATGGGACCAATTGTATG
ACACTGGTAGACAAGGTGGGCCGGGCCAACGACCTCACCATTGATTATGCCGACCAGCGA

Please replace the paragraph at page 83, lines 1-11 as follows:

The oligonucleotides designed for Zmax1 are given below:

10875: AGUACAGCUUCUUGCCAACCCAGUC (SEQ ID NO: 71)

10876: UCCUCCAGGUCGAUGGUCAGCCCAU

(SEQ ID NO: 72)

10877: GUCUGAGUCCGAGUUCAAAUCCAGG (SEQ ID NO: 73)

Figure 13 shows the results of antisense inhibition of Zmax1 in MC3T3 cells. The three oligonucleotides shown above were transfected into MC3T3 and RNA was isolated according to standard procedures. Northern analysis clearly shows markedly lower steady state levels of the Zmax1 transcript while the control gene GAPDH remained unchanged. Thus, antisense technology using the primers described above allows for the study of the role of Zmax1 expression on bone biology. Similar primers can be used to study Zmax1 expression and its ability to regulate lipid levels in an animal.

Attachment to the Response Dated February 3, 2003
Marked-Up Amendments

IN THE CLAIMS

Please amend claim 6 as follows:

6. (Twice Amended) A method for identification of a candidate molecule involved in lipid regulation comprising:

(A) identifying a first molecule that binds to, or that inhibits binding of a second molecule to, the nucleic acid sequence of a Zmax1 nucleic acid chosen from among the sequence SEQ ID NO: 1 and a Zmax1 nucleic acid comprising a polymorphism of Table 4, except for the C/A base change at location 21119 (308G), or a HBM nucleic acid having SEQ ID NO: 2;

(B) measuring the binding of the first molecule, or inhibition of the binding of the second molecule, to the other of either the Zmax1 nucleic acid or the HBM nucleic acid; and,

[(B) identifying a molecule that binds to, or that inhibits binding of a molecule to, the nucleic acid sequence of SEQ ID NO: 2; and]

(C) comparing the extent of binding[, or the extent of inhibition of binding,] of the first molecule, or the extent of inhibition of binding the second molecule, to each nucleic acid sequence, wherein the molecule that binds, or inhibits binding, more or less to the HBM nucleic acid sequence of SEQ ID NO: 2 or the Zmax1 nucleic acid sequence of SEQ ID NO: 1 or a Zmax1 nucleic acid comprising a polymorphism of Table 4, except for the C/A base change at location 21119 (308G), is the candidate molecule.